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Diabetes, hypertension, overweight and hyperlipidemia and 7-day case-fatality in first myocardial infarction

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ABSTRACT

Background: Out-of-hospital deaths due to a first myocardial infarction (MI) are frequent and a big challenge for prevention. Increased knowledge about factors influencing MI fatality is needed. Metabolic risk factors have been studied in relation to MI fatality in-hospital but studies considering also out-of-hospital deaths are few.
Aim: To assess how diabetes and other metabolic risk factors associate with death within 7 days after first time MI among subjects aged between 45 and 70 identified in Stockholm County 1992–1994.
Methods: Data were collected using questionnaires (close relatives of fatal cases were asked to fill the questionnaire), physical examinations, national registers and autopsy reports. Risk ratios (RR) of 7-day MI fatality with 95% confidence intervals (CI) associated with the risk factors under study were calculated using binomial regression with log link.
Results: Out of 1905 first time MI cases included, 524 died within 7 days. After adjustments for age, sex, current smoking, education and general comorbidity, diabetes, but not hypertension and hyperlipidemia, was associated with MI fatality (RR 1.68, 95% CI 1.20–2.28). Overweight, as compared to normal BMI, was inversely associated with MI fatality (multiple adjusted RR 0.68, 95% CI 0.49–0.94); obesity results pointed in the same direction (multiple adjusted RR 0.79, 0.52–1.16).
Conclusions: In this population-based inception cohort study, diabetes but not hypertension and hyperlipidemia were associated with MI fatality. This further emphasizes the importance of diabetes as a cardiovascular risk factor and the need for close surveillance of diabetic patients. Overweight was however associated with decreased MI fatality.

1. Introduction

Although coronary heart disease (CHD) mortality shows a declining trend in different populations [1–4], the proportion of individuals who die within 28 days from the onset of a first myocardial infarction (MI) is still approximately 30% [1,2]. The majority of these individuals die out-of-hospital [1]. The knowledge about determinants of MI fatality is limited. Among the traditional cardiovascular risk factors studied in relation to MI fatality, diabetes has gained most attention.

Diabetes was consistently identified as an important risk factor of in-hospital MI fatality [5–12]. Studies that considered also out-of-hospital CHD deaths (referred to here as population based studies) either support diabetes as a risk factor of MI fatality [9,10] or could not assess it due to limited sample size [13,14]. None of the population based studies used a narrow definition of MI death out-of-hospital; they used any CHD or sudden death [9,10,13,14]. Further, none of these studies considered overweight and obesity as potential confounding factors. Considering the substantial proportion of CHD deaths occurring out-of-hospital [15], further studies are needed to clarify the role that diabetes has in MI fatality. It is also important to elucidate whether other metabolic factors such as hypertension, hyperlipidemia, overweight, and obesity influence MI fatality. Among previous investigations of these factors, only a limited number considered out-of-hospital CHD death, and they regarded only hypertension [13–14,16] and hyperlipidemia [13]. Results point in different directions.

Typically, previous studies of determinants of MI fatality that did consider out-of-hospital CHD death are cohort studies where the assessment of each respective metabolic risk factor took place many years before the MI event. Thus, exposure information may not accurately

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mirror the exposure situation at the time of the MI event. Further, previous studies rarely report the proportion of autopsies forming basis for the classification of MI death. Differentiation between fatal MI and sudden death due to other reasons than MI usually requires autopsy [17].

In the present study, we aimed to assess how diabetes, hypertension, hyperlipidemia, overweight, and obesity, measured close in time to a first MI event, are associated with MI fatality. Although each of these metabolic risk factors has previously been studied in relation to MI fatality, results were most often based solely on admitted MI patients, which may have affected generalizability of results. The present study considers both in- and out-of-hospital deaths. The data forming basis for our study were collected between 1992 and 1994 when the rate of autopsies in Sweden was high: 72% of the fatal MI cases included were ascertained through autopsy.

2. Materials and methods

2.1. Study population

This study is based on material from the Stockholm Heart Epidemiology Program (SHEEP), a study of risk factors for MI performed in Stockholm County among men and women 45–70 years old, residing in Stockholm and who were Swedish citizens. Details about the SHEEP design, including criteria for diagnosis of MI, have earlier been described [18]. Eligible for inclusion in the present inception cohort study were all individuals suffering an MI between 1992 and 1994 in the defined study population without previous hospitalization for MI (International Classification of Diseases, ICD, versions 8 and 9, codes 410 or 412 according to data from the National Patient Register). An additional effort to exclude individuals with previous MI involved asking (using questionnaires) participants whether they had previously been hospitalized due to MI. Those who answered “yes” were phoned and excluded if the prior MI diagnosis was confirmed. MI cases with previous MI, as identified from autopsy reports, but without previous hospitalization for MI recorded were not excluded. Thus, our study is restricted to first known MI cases.

In the SHEEP, 2246 MI cases were identified with a first time documented MI using three sources: 1) coronary units and internal medicine wards for acute care in all Stockholm hospitals; 2) the National Patient Register (ICD 9 code 410 as main or secondary diagnosis); and 3) death certificates (ICD 9 code 410 as main or contributory cause of death) [18]. In the original SHEEP study design, fatal MI was defined as death within 28 days. In 28-day fatal MI cases, MI as a cause of death was ascertained by autopsy data in 69%. The remaining cases were carefully evaluated by the SHEEP secretariat using any available information on disease history and death circumstances. Among the identified cases, 1643 MI cases survived at least 28 days and were considered as non-fatal cases, whereas 603 were considered fatal.

For the main analyses of the current study, we considered as fatal cases only those cases who died out-of-hospital ($n = 203$), died at the emergency department ($n = 170$), or died at hospital within 7 days after MI onset ($n = 151$). Deaths in the latter group occurred either at intensive care units ($n = 59$), internal medicine wards ($n = 35$) or any other ward ($n = 57$). These fatal cases ($n = 524$) we hereafter refer to as 7-day fatal cases. For supplementary analyses, we considered 28-day fatal cases, comprising the 7-day fatal cases and 79 hospitalized MI cases who died between day 7 and day 28 after the event. Among the 7-day fatal cases who were hospitalized and for whom clinical log data were available ($n = 42$), the median hospitalization time was 3 days (interquartile range 2–5 days); for non-fatal cases it was 6 days (interquartile range 5–8 days, $n = 1272$).

The proportion of autopsies among 7-day fatal cases, according to the death certificates, was 72%. From county council archives (mainly Stockholm County) and from forensic medicine departments (in Stockholm, except from one autopsy that took place in Uppsala), we retrieved 49% ($n = 186$) of the autopsy reports pertaining to 7-day fatal cases. Among the 186 autopsy reports retrieved, 37% were performed by forensic pathologists. The main reason for not retrieving reports from autopsies was that reports sometimes had been discarded due to local restrictions regarding long-term archiving. The missing reports should be a random sample of all autopsies.

All participating non-fatal cases were requested to complete a questionnaire which included questions about life style, body habitus, environmental exposures, psychosocial environment, personal history of disease and family history of disease. Participants were also invited to attend a physical examination which took place on average 6 months after the MI event.

2.2. Information about exposures and medical conditions

Most of the data forming bases for this study were retrieved from questionnaires. The vast majority of non-fatal MI cases filled the questionnaires themselves. When the index case could not be contacted or was too ill to fill the questionnaire, a relative was identified and asked to fill the questionnaire in place of the case. The questionnaire was filled by relatives in most of the fatal cases (99.7%) and in a few non-fatal cases (1.5%). The relatives were chosen according to the following priority order: 1) spouse or common-law spouse (49.5%), 2) children older than 18 years old (33.6%), 3) siblings if they were younger than 80 years old (11.0%), 4) parents if they were younger than 80 years old (0.5%), and 5) more distant relatives/friends (5.4%).

The proportion of non-fatal cases participating in SHEEP through completing the questionnaire was 84% whereas in proxies to fatal cases it was 62%. The numbers of MI cases forming basis for the main analyses were 524 7-day fatal cases and 1381 non-fatal cases. The number of participants forming basis for supplementary analyses were 603 28-day fatal cases and 1381 non-fatal MI cases.

Three additional sources were used for retrieving exposure information in the present study: 1) physical examinations (available in 92% of participating non-fatal cases), 2) national registers providing data on diagnoses at previous hospitalizations, number of previous hospitalizations and individual disposable income, 3) autopsy reports (available in 36% of 7-day fatal cases). The information retrieved from autopsy reports was, with the exception of BMI, in general based on either clinical records or statements from close relatives.

2.3. Variable definitions

Diabetes was considered present based on either 1) questionnaire data (report of the presence of diabetes, or report of use of antidiabetic medication), 2) register data (main or secondary hospital diagnosis of diabetes [ICD-8 or ICD-9 code 250] at any time before MI diagnosis), or 3) autopsy report data. Hypertension and hyperlipidemia were correspondingly identified. The ICD-8 and ICD-9 codes used for identifying diagnoses of hypertension were 401–404; for identifying hyperlipidemia code 272 was used.

Body mass index (BMI) was calculated from questionnaire data on weight in kilograms and height in centimeters. However, if such information was available from autopsy (27% of 7-day fatal cases with retrieved autopsy reports) or physical examination (83% of non-fatal cases) that information was used. Overweight was defined as a BMI value between 25 kg/m^2 and 30 kg/m^2, whereas obesity was defined as a BMI of 30 kg/m^2 or above. Individuals with BMI greater than or equal to 18 kg/m^2, but less than 25 kg/m^2 were considered having “normal BMI”, and formed the reference category. Individuals with BMI less than 18 kg/m2 ($n = 25$) were considered underweight and were excluded from the analyses of overweight and obesity.

Previous angina, heart failure, stroke, and intermittent claudication were identified using questionnaire data, data retrieved from autopsy reports or register-based information (main or secondary diagnosis) using the following ICD 8 and ICD 9 codes: 411 and 414 (angina), 428 (heart failure), 430–438 (stroke) and 440C (intermittent claudication).